

Notice of Allowability

Application No.

10/828,479

Applicant(s)

JOHNSON, MICHAEL R.

Examiner

Zachary C. Tucker

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 5 January 2007.
2. ☒ The allowed claim(s) is/are 125-130, 132-161, 164-210 and 212-246.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone conversation between the examiner and applicants' solicitor, James J. Kelly, on 22 March 2007.

IN THE CLAIMS -

In claim 125, in line 9 on page 4 of the Preliminary Amendment filed 4 November 2004, the language --restoring mucosal defense, preventing-- has been deleted, and in place thereof, the phrase "treatment of" has been inserted.

In claim 125, in line 16 of page 4 of the Preliminary Amendment filed 4 November 2004, the word "comprising" has been inserted before the word "administering."

In claim 125, in lines 6 and 7 on page 9 of the Preliminary Amendment filed 4 November 2004, the language --or a nitrogen atom, wherein at most 3 Q in a ring is a nitrogen atom;-- has been deleted.

In claim 132, in line 4 on page 10 of the Preliminary Amendment filed 4 November 2004, the word --preventing-- has been deleted, and the phrase "treatment of" has been inserted in its place.

In claim 208, in line 7 on page 24 of the Preliminary Amendment filed 4 November 2004, the language --at most 2 Q in a ring are nitrogen atoms-- has been deleted.

In claim 210, in line 14 on page 24 of the Preliminary Amendment filed 4 November 2004, the language --at most 1 Q in a ring is a nitrogen atom-- has been deleted.

Claims 131, 162, 163 and 211 have been **cancelled**.

end of amendments

Requirement for Restriction

A Requirement for Restriction, represented in written form, was mailed to applicants' counsel on 5 December 2006. In reply to that Requirement, applicants, *via* counsel, indicated election of the invention of Group I, the method wherein the formula (I) compound administered to the subject is comprised of a "Q" variable-containing ring which is a phenyl ring (as opposed to those formula (I) compounds wherein said ring is a pyridine, 1,2-diazine, 1,3-diazine, 1,2,4-triazine or 1,3,5-triazine).

No traversal of the Requirement was voiced in applicants' response.

Non-elected subject matter is struck from the claims by virtue of the attached Examiner's Amendment authorized by applicants' counsel; the claims are allowed.

Allowable Subject Matter

Claims 125-130, 132-161, 164-210 and 212-246 are allowed.

The following is an examiner's statement of reasons for allowance:

Compounds as described by formula (I) according to the method of instant claim 125 are not disclosed in the prior art in any reference suggesting that any effect specified in claim 125 is attainable with said compounds. Only those compounds according to formula (I) of instant claim 125 wherein R^5 is $-(CH_2)_n-CO_2R^7$, R^7 being either hydrogen or methyl, are disclosed in the prior art. These two embodiments of the compounds of formula (I) are disclosed in Kleyman et al, *American Journal of Physiology*, vol. 260(2, Pt. 1), pages C271-C276 (1991) and Cocks et al, *British Journal of Pharmacology*, vol. 95(1), pages 67-76 (1988), respectively. Neither Kleyman et al nor Cocks et al, however, suggest any specific therapeutic utility for the compounds. In the patent which issued from the parent application to the instant application (parent application was serial number 10/076,571), US 6,858,615, the alternative $-(CH_2)_n-CO_2R^7$ was deleted from the definition

Art Unit: 1624

of R⁵, in the claims drawn to the formula (I) compounds *per se*, because the Kleyman et al and Cocks et al references were anticipatory with respect to formula (I) compounds where R⁵ is $-(CH_2)_n-CO_2R^7$.

Also pertinent prior art with respect to the instant claims are;

Kleyman et al, "The Cellular Pool of Sodium Channels in the Amphibian Cell Line A6 Is Not Altered by Mineralocorticoids. Analysis Using a New Photoactive Amiloride Analog in Combination with Anti-Amiloride Antibodies" *Journal of Biological Chemistry*, vol. 264(20), pages 11995-20000 (1989).

Epand et al, "Reversal of Intrinsic Multidrug Resistance in Chinese Hamster Ovary Cells by Amiloride Analogs" *British Journal of Cancer*, vol. 63(2), pages 247-251 (1991)

and,

US 4,894,376 (Morad and Tang)

each of which disclose compounds similar to those described by formula (I) as set out in instant claim 125. The Kleyman et al (1989) and Epand et al references, in addition to the Kleyman et al (1991) and Cocks et al references relied upon in prior art-based rejections in the parent application, are all cited in the Information Disclosure Statements (IDS) filed in this application 12 July 2006 and 21 April 2004. Morad and Tang is cited on a PTO form 892, submitted herewith; applicants did not cite the patent in an IDS.

Kleyman et al (1989) discloses a compound like a formula (I) compound, except that the phenyl ring corresponding to the "Q" containing ring therein is substituted with a nitro and a methyl group, neither which are not part of the definition of R⁵ (page 11996 of the reference).

Epand et al discloses a compound like those described by formula (I) as set out in instant claim 125, except that the phenyl ring corresponding to the "Q" containing ring therein is substituted with either two chlorine atoms, two methyl groups, a trifluoromethyl group, or a hydroxyl group, none of which are permitted in the definition of R⁵ (see table on page 249 of the reference).

Art Unit: 1624

The Morad and Tang patent teaches treatment of central nervous system disorders with 3,4-dimethoxybenzamil, a compound similar to the formula (I) compounds specified in the method according to instant claim 125. Formula (I) does not provide for dimethoxy substitution on the "Q" containing ring (which is phenyl).

A claim drawn to blocking (cellular) sodium channels, comprising contacting sodium channels with a compound of formula (I) as set forth in instant claim 125, is patented in US 6,858,615 ("parent patent"), which issued from the parent application to the instant application, but since a Requirement for Restriction issued in the prosecution of that application established that methods according to instant claim 125 as being patentably distinct from a method of blocking sodium channels, no finding of Obviousness-Type Double Patenting of the instant claims, over claims of the parent patent,, is proper in the instant application.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

All Post-Allowance Correspondence concerning this application must be mailed to:
Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Or you can fax them to the Office of Patent Publications at 703-872-9306, in order to expedite the handling of such correspondence as amendments under 37 CFR 1.312; information disclosure statements, and formal drawings. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at (703) 305-8027. The Notice of Allowance also has an insert containing contact information on other items, including Issue Fees, receipt of formal drawings and the status of the application.



ZACHARY C. TUCKER
PRIMARY EXAMINER